THE PREPARATION AND ANTISCORBUTIC PROPERTIES OF CERTAIN ASCORBIC ACID DERIVATIVES

BY

MILDRED CATHERINE REBSTOCK

B. A., North Central College, 1942

M. A., University of Illinois, 1943

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
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THE PREPARATION AND ANTISCORBUTIC PROPERTIES OF CERTAIN ASCORBIC ACID DERIVATIVES

PART I

GENERAL INTRODUCTION

Few ascorbic acid derivatives in which the enediol system has been stabilized by substitution with organic radicals have been prepared. Not only would such compounds with vitamin C activity be of practical value, but the study of these substances might lead to information about the metabolism of ascorbic acid, concerning which little is known.

PART II

THE PREPARATION AND ANTISCORBUTIC PROPERTIES OF 3-METHYL *l*-ASCORBIC ACID

INTRODUCTION

The compound, 3-methyl *l*-ascorbic acid, is a vinylogous ester of ascorbic acid in which the enediol system has been stabilized by substitution. The preparation of this derivative was described in 1934 by Reichstein and coworkers[1] and Haworth and Hirst[2]. A report by Bezssonov and Sacrez[3]. indicating that the compound might possess antiscorbutic properties, suggested the need for a comprehensive study of the biological activity of the substance.

EXPERIMENTAL

Crystalline 3-methyl *l*-ascorbic acid was prepared in quantity for use in chemical and physiological studies. The derivative was administered daily to young male guinea pigs at levels of five, ten, and twenty milligrams in experiments designed to demonstrate the efficacy of the compound both in curing and preventing scurvy. A comparison was made of the relative effectiveness of oral administration and intra-

peritoneal injection. To determine the adequacy of the various supplements, daily weight records, observations of the gross appearance of the animals, and determinations of blood and adrenal ascorbic acid levels at the conclusion of the experimental periods were made. The method described by Roe and Kuether[4] was employed in these determinations.

The results of this work have demonstrated that 3-methyl *l*-ascorbic acid can be utilized by the guinea pig. Intraperitoneal injection has proved to be quantitatively superior to oral administration. Daily supplements of twenty milligrams by the former route resulted in normal growth for a period of seventy-five days, but observations of the behavior of the animals, together with a consideration of the blood and adrenal ascorbic acid levels, have indicated that this dosage is slightly subminimal. The results of curative experiments have supported this conclusion.

Experiments designed to demonstrate the metabolic fate of the compound have been inconclusive, but indirect evidence indicating that hydrolysis (probably enzymatic) is necessary before the compound can be utilized has been obtained.

SUMMARY

The compound, 3-methyl *l*-absorbic acid, has been shown to possses marked antiscorbutic properties. A quantity of twenty milligrams administered daily by intraperitoneal injection provides slightly less than the minimum requirement of ascorbic acid. A tentative hypothesis based on considerable indirect evidence has suggested that hydrolysis is the first step in the utilization of 3-methyl *l*-ascorbic acid by the guinea pig.

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PART III

THE PREPARATION, STRUCTURE, AND ANTISCORBUTIC PROPERTIES OF PHENACYL AND PARA-SUBSTITUTED PHENACYL ASCORBIC ACIDS

INTRODUCTION

The use of phenacyl halides and substituted phenacyl halides for the esterification of numerous organic acids has been studied by Reid and coworkers[1,2,3]. The possibility that these reagents would react with ascorbic acid to produce substitution in the enediol system and thus stabilize the compound provided the stimulus for this work.

EXPERIMENTAL

The reaction of phenacyl bromide, *p*-bromophenacyl bromide, and *p*-phenylphenacyl bromide with *l*-ascorbic acid yielded crystalline derivatives. By means of qualitative organic tests, microanalytical data, and the preparation and analysis of derivatives, these compounds were shown to be 2,3-disubstituted ascorbic acids. Diacetyl, dibenzoyl, and isopropylidene derivatives were those prepared.

The antiscorbutic properties of 2,3-diphenacyl *l*-ascorbic acid were tested by oral administration of twenty, forty, and sixty milligram levels of the derivative daily to young female guinea pigs. While the compound did not appear to be toxic, it was found to be totally ineffective both in preventing and curing scurvy.

SUMMARY

New derivatives of ascorbic acid have been prepared. These have been shown to be 2,3-diphenacyl *l*-ascorbic acid, 2,3-di-*p*-bromophenacyl *l*-ascorbic acid, and 2,3-di-*p*-phenylphenacyl *l*-ascorbic acid.

The compound, 2,3-diphenacyl *l*-ascorbic acid has been shown to possess no vitamin C activity in doses up to sixty milligrams per day when administered by mouth to young guinea pigs.

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VITA

The author was born November 29, 1919, in Elkhart, Indiana. She received her elementary and secondary education in the Elkhart Public Schools. From September, 1938, to June, 1942, she attended North Central College at Naperville, Illinois, receiving the Bachelor of Arts Degree in chemistry and zoölogy. At that time she was awarded a scholarship by the University of Illinois and the following September entered the graduate school. In October, 1943, she received the Master of Arts Degree in chemistry. Second and third year fellowships were granted for the spring and fall semesters of 1943 and 1944. During the summers of these years she was employed as a Special Research Assistant with grants from the S. M. A. Corporation. She also held a Teaching Assistantship in Chemistry during the summer of 1944.

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